Remarks

The Office Action mailed June 28, 2005 has been received and reviewed. Claims 35 and 36 having been amended, the pending claims are claims 2-5, 7-11, and 17-39. Claims 17-28 being withdrawn from examination, as drawn to non-elected inventions, the claims presently under examination are claims 2-5, 7-11, and 29-39. Reconsideration and withdrawal of the rejections are respectfully requested.

Examiner Interview

A telephonic Examiner's Interview was held between Examiner Szperka and Applicant's Representative, Nancy Johnson, in which the appropriateness of the finality of the Office Action mailed May 26, 2005, was discussed. Applicants thank the Examiner for the courtesy of this interview and acknowledge the Examiner's reconsideration of the finality of the Office Action and the issuance of the replacement, non-final Office Action, mailed June 28, 2005.

Information Disclosure Statement

In reviewing a copy of the Information Disclosure Statement (mailed March 22, 2005) included with the Office Action mailed May 26, 2005, Applicants note that, although the Examiner has signed and dated the overall PTO-1449, he has not initialed, as considered, any of the individual U.S. Patent Documents listed on the document. Applicants request that the Examiner consider and initial each of various documents included on the Information Disclosure Statement (mailed March 22, 2005). To assist the Examiner, a copy of the PTO-1449 (mailed March 22, 2005) is enclosed.

Restriction Requirement

Applicants continue to traverse the Restriction Requirement mailed July 1, 2004 and respectfully request the rejoinder and examination of claims 27 and 28 (Group III) along with the elected claims of Group I. Claims 27 and 28 are drawn to a "fertility impairing vaccine

comprising an avian zona pellucida protein or an immunogenic fragment thereof and a porcine zona pellucida protein or an immunogenic fragment thereof." As explained in the specification on page 2, lines 9-29, the preparation and use of porcine zona pellucida protein (pZP) as a vaccine is known, with pZP having "been used for more than eight years in horses with no known adverse effects" (page 2, lines 16-17 of the specification). Applicants respectfully submit that the burden of searching and examining claims 27 and 28 along with claims 2-5 and 7-11 is not undue. Rejoinder and examination of claims 27 and 28 is respectfully requested.

The 35 U.S.C. §112, First Paragraph, Rejection

The Examiner rejected claims 2-5, 7-11, and 29-39 under 35 U.S.C. §112, first paragraph, alleging the specification does not contain a written description of the claimed "immunogenic fragments." Applicants respectfully disagree and traverse this rejection.

Claims 2-5, 7-11, and 29-39 are drawn to "an immunogenic fragment thereof" of an avian zona pellucida protein. Applicants submit that information which is well known in the art need not be described in detail in the specification. See, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1379-80, 231 USPQ 81, 90 (Fed. Cir. 1986)(M.P.E.P. § 2163). Applicants submit that the level of knowledge and skill in the art of immunology and vaccine preparation is very high and that the preparation and inclusion of immunogenic fragments of a protein, such as avian zona pellucida protein, in a vaccine would be routine for one of skill in the art, at the time of the instant invention. See, for example, the various vaccines including immunogenic fragments as claimed in U.S. Patent Nos. 5,171,568, 5,840,315, 5,843,460, 5,869,066, 5,897,475, and 5, 976,525.

Applicants submit that the specification provides adequate written description for the claimed "immunogenic fragment thereof." As described in the specification, "[a]n immunogenic fragment of an avian zona pellucida protein . . . is a peptide fragment . . that elicits an immune response in a subject to which it is administered. An immune response includes either or both a cellular immune response or production of antibodies . . . . For example,

an immune response is evidenced by a detectable anti-aZP antibody level in the subject using ELISA" (page 5, line 27 to page 6, line 2 of the specification). Further, with Examples III and IV, the specification provides working examples of methods of determining antibody titer (page 16, lines 16-28 and page 17, lines 11-24) that can be used to identify immunogenic fragments of an avian zona pellucida protein.

The Examiner asserted that "the specification does not teach which regions of avian zona pellucida proteins contain immunogenic fragments, or if the sequences and structures of the immunogenic fragments are conserved among zona pellucida proteins isolated from any avian" (pages 3-4 of Office Action mailed June 28, 2005). Applicants respectfully submit, as detailed in the paragraph above, that one of skill in the art does not need such information on the amino acid sequence of a protein, the three dimensional structure of a protein, or the comparison between the same protein obtained from different species in order to prepare immunogenic fragments thereof of a protein. In fact, the Examiner acknowledges as much with the assertion that, "[w]hile it may be possible to screen for such immunogenic fragments, applicant has not indicated the starting material to be used in to begin such a screening assay, and has not indicated the sequence or structure that would be obtained upon completion of said assay" (pages 3-4 of Office Action mailed June 28, 2005). In answer to the Examiner's questions, the claims are drawn to a "zona pellucida protein or an immunogenic fragment thereof," and the original "starting material" for the claimed "immunogenic fragments thereof" is avian zona pellucida protein. Further, as already discussed, immunogenic fragments are routinely made without knowledge of the sequence or structure of the protein and fragments of the protein.

In view of the above discussion, Applicants respectfully submit that the specification provides adequate written description for the claimed "immunogenic fragments thereof." Reconsideration and withdrawal of this rejection 35 U.S.C. §112, first paragraph, under is requested.

The 35 U.S.C. §102 Rejection

The Examiner rejected new claims 34-38 under 35 U.S.C. §102(a) as being anticipated by Waclawek et al. (Biology of Reproduction, 1998: 59:1230-1239. Applicants respectfully traverse this rejection.

Specifically, the Examiner asserted that Waclawek et al. discloses a polypeptide with an apparent molecular weight that can vary between 34 kD and 43 kD, and "[a]s such, the chZPC used by Waclawek et al. to vaccinate rabbits and generate an antibody response contains avian zona pellucida protein of apparent molecular weights 35 and 40 kD" (pages 5 and 6, Office Action mailed June 28, 2005) and thus is the same as claims 34-38. Applicants respectfully disagree.

Claims 35 and 36 have been amended to depend from claim 29. Thus, the fertility impairing vaccines of claims 35 and 36 comprise "an immunological adjuvant selected from the group consisting of aluminum hydroxide, Acemannan, permulum, synthetic trehalose dicorynomycolate, squalene oil, drakeol, vegetable oil, lecithin, phosphtidyl choline, and combinations thereof." Applicants respectfully submit that Waclawek et al. does not teach these adjuvants. Thus, Waclawek et al. does not teach all of the limitations of claims 35 and 36. Waclawek et al. does not anticipate claims 35 and 36.

With respect to claims 34, the Examiner asserted that "the chZPC isolated by Waclawek et al. is immunogenic and as such is considered to be a fragment of the 70 kD zona pellucida protein (and is also a fragment of the 40 kD and 35 kD zona pellucida proteins as well) (page 5 and 6, Office Action mailed June 28, 2005). Applicants respectfully disagree and submit that there is no basis for the Examiner's conclusion that the polypeptide taught by Waclawek et al. is a fragment of the 70 kD protein recited in claims 34 and 37. As shown in Example I, the total avian zona pellucida protein preparation used in the present invention includes a plurality of at least three distinct proteins, having molecular weights of 70 kD, 40 kD, and 35 kD (see page 5, lines 1-7 and page 15, lines 1-9). If the Examiner continues to maintain this rejection,

Applicants request that the Examiner provide clear evidence of fragmentation of the 70 kD protein to produce either or both of the smaller proteins.

Finally, with respect to claims 37 and 38, Applicants submit that Waclawek et al. does not teach a "vaccine comprising two, but not three . . . of . . . a 40 kD avian zona pellucida protein . . . a 35 kD avian zona pellucida protein . . . and a 70 kD avian zona pellucida protein" (claim 37) or a vaccine comprising "a 40 kD avian zona pellucida protein or an immunogenic fragment thereof, and a 35 kD avian zona pellucida protein or an immunogenic fragment thereof, and does not comprise a 70 kD avian zona pellucida protein or an immunogenic fragment thereof" (claim 38). Thus, Waclawek et al. does not anticipate claims 37 and 38.

In view of the above discussion, reconsideration and withdrawal of this rejection under 35 U.S.C. §102(a) is respectfully requested.

The 35 U.S.C. §103 Rejection over Waclawek in view of Cox

The Examiner rejected claims 2-5, 10, 11, 29, 31, and 32 as being unpatentable under 35 U.S.C. §103 over Waclawek et al. in view of Cox et al. (Vaccine (1997) 15:248-256). This rejection is respectfully traversed.

Specifically, the Examiner asserted that while Waclawek et al. does "not teach the adjuvants recited in claim 29 as part of a chZPC vaccine composition that induces an antibody response when administered to rabbits. Cox et al. teach that aluminum salt, notably aluminum hydroxides, have been widely used in human and veterinary vaccines" (page 7, Office Action mailed June 28, 2005). The Examiner asserted that one of ordinary skill in the art at the time of the invention would have been motivated to combine the teachings of Waclawek et al. and Cox et al., to substitute the Freund's adjuvant taught by Waclawek et al. with the aluminum hydroxide adjuvant taught by Cox et al. "to gain the advantages of inducing a strong antibody response, low cost, safety, and ease of formulation as taught by Cox et al." (Page 8, Office Action mailed June 28, 2005). Applicants disagree.

Waclawek et al. teaches that "[r]abbit anti-chZPC antibodies were raised by three series of intradermal injections each of 500 g chZPC in 400 µl elution buffer, mixed with an equal volume of Freund's complete . . . or incomplete adjuvant" (see col. 1, page 1231). Waclawek et al. teaches that the rabbit polyclonal antisera produced by this immunization was used as a research reagent in the electrophoretic and western blot analysis of chicken perivitelline membrane (pvm), the immunoprecipitation of biosynthetically labeled chZP3, and the immunohistochemical localization of chZP3 in follicle tissue sections (see col. 1, page 1231 to col 2, page 1232 and Figs. 1, 4-7). Thus, Waclawek et al. teaches immunization with a composition of chZPC and Freund's adjuvant for the generation of polyclonal antisera in a laboratory animal (a rabbit). The resultant antisera was successfully used as research reagent in the laboratory analysis of chZPC by western blot, immunoprecipitation, and immunohistochemistry. Waclawek et al. does not teach or suggest compositions of chZPC for purposes of *therapeutic* immunization, that is for use as a vaccine.

Cox et al. teaches that "various substances have been added to vaccines and certain formulations have been devised in an attempt to render vaccines more effective" (abstract) and that the aluminum salts, including aluminum hydroxides, "have been widely used in human and veterinary vaccines" (250, column 2).

According to M.P.E.P. § 2143.01, "[o]bviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either explicitly or implicitly in the references themselves or in the knowledge generally available to one of ordinary skill in the art." Applicants respectfully submit that no such teaching, suggestion, or motivation to combine the teachings of Waclawek et al. or Cox et al. is found either explicitly or implicitly in the references themselves or in the knowledge generally available to one of ordinary skill in the art to arrive at the claimed invention.

Waclawek et al. teaches a composition of chZPC and Freund's adjuvant and its use as an immunogen for the successful generation of polyclonal antisera for use as a laboratory reagent.

Applicants submit that one of ordinary skill in the art would not be motivated to alter the composition taught by Waclawek et al. In particular, one of ordinary skill in the art would not be motivated to combine the teachings of Waclawek et al. and Cox et al., to render the composition taught by Waclawek et al. more effective as a vaccine for human or veterinary use, as taught by Cox et al.

Applicants respectfully submit that as there is no recognition in Waclawek et al. of the potential therapeutic uses of an avian zona pellucida vaccine, there is no teaching, suggestion, or motivation to combine the teachings of Waclawek et al. and Cox et al. found either explicitly or implicitly in the references themselves or in the knowledge generally available to one of ordinary skill in the art to arrive at the claimed invention. Reconsideration and withdrawal of this rejection of the claims under U.S.C. §103 is requested.

The 35 U.S.C. §103 Rejection over Waclawek in view of Willis

The Examiner rejected claims 2-5, 7, 8, 10, 11, 29, 31, and 33 as being unpatentable under 35 U.S.C. §103 over Waclawek et al. in view of Willis et al. (J. Equine Vet. Sci., (1994) 14:364-370). This rejection is respectfully traversed.

Specifically, the Examiner asserted that the teachings of Waclawek et al. "differ from the claimed invention in that Waclawek et al. do not [use] the adjuvants synthetic trehalose dicorynomycolate or squalene oil in their vaccine composition comprising chZPC that induces an antibody response" (page 8, Office Action mailed June 28, 2005). However, the Examiner asserted that "Willis et al. teach the use of synthetic trehalose dicorynomycolate and squalene oil as adjuvants for delivery of a vaccination via a biobullet" (page 8, Office Action mailed June 28, 2005).

The Examiner asserted "a person of ordinary skill in the art would . . . have been motivated . . . to deliver the chZPC vaccine of Waclawek et al. via a biobullet to gain the advantages of maximized treatment efficiency with minimized danger and harassment of the animal as taught by Willis et al." (page 9, Office Action mailed June 28, 2005). Applicants

respectfully disagree. Willis et al. teaches the use of biobullets for remote vaccine delivery to feral horse populations (abstract). There is no recognition in Waclawek et al. of the potential therapeutic possibilities of an avian zona pellucida vaccine. Applicants submit that one of ordinary skill in the art would not be motivated to combine such teachings, on the use of biobullets, with the deliver of an immunogenic composition to a laboratory rabbit housed in a cage within an animal facility, as taught by Waclawek et al. Applicants respectfully submit that there is no teaching, suggestion, or motivation to combine the teachings of Waclawek et al. and Willis et al. found either explicitly or implicitly in the references themselves or in the knowledge generally available to one of ordinary skill in the art to arrive at the claimed invention.

The Examiner asserted that "a person of ordinary skill in the art would have been motivated . . . to substitute synthetic trehalose dicorynomycolate and squalene oil for Freund's adjuvant in the vaccine compositions of Waclawek et al. for the advantage of minimizing unwanted side effects such as vaccination site abscess formation as taught by Willis et al." (page 9, Office Action mailed June 28, 2005). Applicants disagree. There is no recognition in Waclawek et al. of the potential therapeutic possibilities of an avian zona pellucida vaccine. Willis et al. teaches vaccines emulsified with synthetic trehalose dicorynomycolate and squalene oil (TDM adjuvant) "packaged in a biobullet for remote delivery. This was in contrast to previous reports using Freund's adjuvant and a dart when administered remotely. Advantages of the new method included the finding that the biobullets/TDM adjuvant vaccination used in this study did not result in abscess formation" (page 369, second complete paragraph). Applicants respectfully submit that Willis et al. teaches that replacing the dart/Freund's adjuvant combination with the biobullet/TDM adjuvant combination prevents abscess formation. Applicants respectfully submit that one of ordinary skill in the art would not be motivated to make such a substitution, substituting a dart/Freund's adjuvant combination with a biobullet/TDM combination, in the teachings of Waclawek et al.

Applicants respectfully submit that no teaching, suggestion, or motivation to combine the teachings of Waclawek et al. and Willis et al. is found either explicitly or implicitly in the

references themselves or in the knowledge generally available to one of ordinary skill in the art to arrive at the claimed invention. Reconsideration and withdrawal of this rejection of the claims under 35 U.S.C. §103 is requested.

The 35 U.S.C. §103 Rejection over Waclawek in view of Dean

The Examiner rejected Claim 30 is rejected as being unpatentable under 35 U.S.C. §103 over Waclawek et al. in view of Dean (U.S. Patent 5,641,487). This rejection is respectfully traversed. Specifically, the Examiner asserted that while Waclawek et al. does not teach "chZPC that has been conjugated to an immunogenic carrier[,] Dean teaches that it is well known to couple antigens to carrier proteins to gain the advantage of enhancing the immune response to the target antigen" (page 9, Office Action mailed June 28, 2005). Applicants respectfully disagree.

Dean teaches that "[i]t is well known that the vast majority of small peptides (containing six to twenty amino acids, for instance) that have been tested for the induction of antibodies are considerably less potent immunogens than the larger proteins from which they are derived . . . Certain chemical modifications of a peptide, particularly coupling of the peptide to a lager proteinaceous 'carrier' generally enhance the immune response to a small peptide" (col. 8, lines 9-18). Waclawek et al. teaches the successful generation of polyclonal antisera after immunization with a preparation of intact chZPC protein and does not teach immunization with small peptides derived from *intact* chZPC protein. There is no recognition in Waclawek et al. of the potential therapeutic possibilities of an avian zona pellucida vaccine. One of ordinary skill would not be motivated to conjugate the *intact* proteins taught by Waclawek et al. to the carriers taught by Dean.

Applicants respectfully submit that no such teaching, suggestion, or motivation to combine the teachings of Waclawek et al. and Dean is found either explicitly or implicitly in the references themselves or in the knowledge generally available to one of ordinary skill in the art

to arrive at the claimed invention. Reconsideration and withdrawal of this rejection of the claims under 35 U.S.C. §103 is requested.

The 35 U.S.C. §103 Rejection Waclawek in view of Bagavant

The Examiner rejected claims 9 and 39 as being unpatentable under 35 U.S.C. §103 over Waclawek et al. in view of Bagavant et al. (Biology of Reproduction (1997), 56:764-770). This rejection is respectfully traversed.

Specifically, the Examiner asserted that Waclawek et al. does not teach the "use of chZPC in a composition that also contains an immune cell epitope from a parasite. [However,] Bagavant et al. teach the use of immune cell epitopes from the malarial circumsporozite protein of *Plasmodium faciparum* as part of a zona pellucida fertility impairing vaccine" (page 10, Office Action mailed June 28, 2005). "Therefore, it would have been obvious . . . to include an immune cell epitope from *P. faciparum* as taught by Bagavant et al. as part of the chZPC vaccine composition taught by Waclawek et al. to ensure a strong antibody response as taught by Bagavant et al. (page 11, Office Action mailed June 28, 2005). Applicants respectfully disagree.

Bagavant et al. teaches that a "contraceptive vaccine that elicits antibodies to zona pellucida (ZP) without concomitant pathogenic T-cell activation has been achieved by a chimeric peptide (CP) consisting of a native ZP3 B-cell epitope and a foreign helper T-cell peptide" (abstract, Bagavant et al.). The chimeric peptides taught by Bagavant et al. are formed by linking short peptides derived from human, macaque, and mouse ZP3 proteins to short peptides derived from *P. faciparum* (see Table 1, Bagavant et al.). Waclawek et al. teaches the successful generation of polyclonal antisera after immunization with a preparation of intact chZPC protein. Waclawek et al. does not teach peptides obtained from the intact chZPC protein. There is no recognition in Waclawek et al. of the potential therapeutic possibilities of an avian zona pellucida vaccine. One of ordinary skill would not be motivated to combine the teachings of Waclawek et al., of immunization with intact chZPC protein, with the teachings of Bagavant

et al., of preparation of chimeric peptides by linking short peptide sequences of short human, macaque, or mouse ZP3 proteins to short peptides derived from *P. faciparum*.

Applicants respectfully submit that no teaching, suggestion, or motivation to combine the teachings of Waclawek et al. and Bagavant et al. is found either explicitly or implicitly in the references themselves or in the knowledge generally available to one of ordinary skill in the art to arrive at the claimed invention. Reconsideration and withdrawal of this rejection of the claims under 35 U.S.C. §103 is requested.

Summary

It is respectfully submitted that the pending claims 2-5, 7-11, and 17-39 are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicants' Representatives, at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted for
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CERTIFICATE UNDER 37 CFR §1.8:
The undersigned hereby certifies that the Transmittal Letter and the paper(s), as described hereinabove, are being transmitted by facsimile in accordance with 37 CFR §1.6(d) to the Patent and Trademark Office, addressed to **Mail Stop Amendment**, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 28 day of NOV., 2005, at 2:50 p.m. (Central Time).

By: Sandy Truehart
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OMB No. 0651-0011

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	Applicant(s): FAYRER-HOSKEN et al.	Confirmation No.: 1056
	Application Filing Date: 02/01/02	Group: 1644
	Information Disclosure Statement mailed: 3-22, 2005	

U.S. PATENT DOCUMENTS

Examiner Initial	Copy Enclosed	Document Number	Date	Name	Class	Subclass	Filing Date If Appropriate
	✔	5,171,568	12/15/92	Burke et al.			
	✔	5,840,315	11/24/98	Leigh			
	✔	5,843,460	1201/98	Labigne et al.			
	✔	5,869,066	02/09/99	Pace et al.			
	✔	5,897,475	04/27/99	Pace et al.			
	✔	5,976,525	11/02/99	Pace et al.			

FOREIGN PATENT DOCUMENTS

Examiner Initial		Document Number	Date	Country	Class	Subclass	Translation	
							Yes	No
		NONE						

OTHER DOCUMENTS (Including Authors, Title, Date, Pertinent Papers, etc.)

Examiner Initial		Document Description
		NONE

EXAMINER	Date Considered

*Examiner: Initial if citation considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.